Mass General Brigham
Health Plan

Medical Necessity Guidelines
Imlygic (talimogene laherparepvec, T-VEC)

Policy Number: 115

Contents

Overview

Imlygic is a genetically modified oncolytic viral therapy for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

FDA-Approved Indication
Imlygic is indicated for:

1. Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions recurrent after initial surgery in patients with melanoma.

Limitations of use: Imlygic has not been shown to improve overall survival or have an effect on visceral metastases.

Medicare Advantage

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, CMS offered the following guidance:**

- **Medicare Benefit Policy Manual Chapter 15: Covered Medical and Other Health Services**

When CMS documentation references FDA labeling, Mass General Brigham Health Plan applies additional coverage criteria to clarify medical necessity of the requested service. Mass General Brigham Health Plan coverage criteria align with the latest clinical evidence and accepted standards of practice, without contradicting

existing determinations, and enhance the clarity of medical necessity criteria, documentation requirements, and clinical indications.

Criteria

1. Criteria for Initial Approval

   Authorization may be granted when all of the following criteria are met:

   a. The member has a diagnosis of unresectable melanoma; and

   b. The melanoma is recurrent after initial surgery; and

   c. The lesions are unresectable, metastatic cutaneous, subcutaneous, and/or nodal.

2. Dosing and Administration

   a. The recommended starting dose is up to 4mL of Imlygic at a concentration of 10^6 (1 million) plaque-forming units (PFU) per mL.

   b. Subsequent doses should be administered up to 4mL at a concentration of 10^8 (100 million) PFU per mL.

Exclusions:

- The member is immunocompromised.
- The member is pregnant.

Mass General Brigham ACO

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses the MassHealth Drug List for medical necessity determinations for members of the Mass General Brigham ACO. Criteria for Imlygic are found in Table 57: Oncology Agents.

One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, or the member does not meet all of the medical necessity criteria for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. **See Medicare Advantage criteria and exclusions above. If Medicare Advantage criteria are not met, then MassHealth criteria are applied.**

Commercial and Qualified Health Plans

Prior Authorization Required	Yes ☒ No ☐

Prior authorization for Imlygic for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See the Prime Therapeutics policy for Imlygic for more information.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Code	Code Description
J9325	Injection, talimogene laherparepvec, per 1 million plaque forming units

Summary of Evidence

Talimogene laherparepvec (T-VEC; Imlygic) is an oncolytic herpesvirus approved for the treatment of unresectable, injectable melanoma lesions, and its clinical role has been increasingly characterized through randomized trials, systematic reviews, and major society guidelines. As a single agent, T-VEC has demonstrated meaningful activity in stage IIIB–IVM1c melanoma, with a meta-analysis reporting a median complete response rate of 40% and median durable response rate of 38% in a meaningful subset of patients (Stahlie et al., 2022). A network meta-analysis further confirmed that T-VEC was associated with improved overall response rates compared to granulocyte-macrophage colony-stimulating factor (GM-CSF) alone, though benefits were most pronounced in patients with earlier-stage disease (Shen et al., 2025). These findings are reflected in current clinical practice guidelines, with both the ASCO Systemic Therapy for Melanoma guideline and the ESMO Clinical Practice Guideline recognizing T-VEC as an option for patients with unresectable stage III–IV melanoma, particularly those with injectable cutaneous, subcutaneous, or nodal lesions (Seth et al., 2023; Amaral et al., 2025).

Combination strategies have been a major focus of T-VEC clinical development, particularly pairing it with immune checkpoint inhibitors. The 5-year final analysis of a phase II trial evaluating T-VEC plus ipilimumab versus ipilimumab alone demonstrated an objective response rate of 39% in the combination arm versus 18% in the ipilimumab-alone arm, with the combination showing a median overall survival of 24.0 months compared to 18.9 months for ipilimumab monotherapy (Chesney et al., 2023). However, the MASTERKEY-115 phase II study of T-VEC combined with pembrolizumab in patients who had progressed on prior anti-PD-1 therapy showed more modest results, with an objective response rate of approximately 11%, suggesting limited benefit for T-VEC-based combinations in the anti-PD-1–refractory setting (Robert et al., 2024). In the neoadjuvant context, a 5-year follow-up of a randomized clinical trial evaluating T-VEC prior to surgery in advanced melanoma reported an event-free survival benefit in the T-VEC-plus-surgery arm compared to surgery alone, with 33.5% versus 21.9% of patients remaining event-free at 5 years, supporting further exploration of T-VEC as a neoadjuvant strategy (Dummer et al., 2023).

Beyond the clinical trial data, T-VEC's role in locoregional disease management is well-established in evidence-based practice resources. The Ontario Health (Cancer Care Ontario) clinical practice guideline identifies intralesional therapy, including T-VEC, as an appropriate option for in-transit melanoma metastases not amenable to complete surgical resection (Wright et al., 2020), a recommendation echoed by the UpToDate review on management of local recurrence and in-transit disease (Tanabe & Tyler, 2026). A Cochrane systematic review on neoadjuvant treatment for stage III–IV cutaneous melanoma acknowledged T-VEC among emerging preoperative strategies, though it noted that the overall evidence base remains limited by small sample sizes and heterogeneity across studies (Gorry et al., 2023). A symplr evidence analysis brief similarly concluded that while T-VEC provides clinically meaningful benefit for a defined subset of melanoma patients, its optimal positioning within the broader treatment landscape, particularly relative to systemic immunotherapy combinations, continues to evolve (symplr Evidence Analysis, 2023).

Effective Dates

August 1, 2026: Effective date.

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